UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,840	05/17/2007	Maureen Caligiuri	GPC-298.1P US	2801

7590 10/05/2009

Leon R. Yankwich, Esq.
Yankwich & Associates, P.C.
201 Broadway
Cambridge, MA 02139

EXAMINER	
PAGONAKIS, ANNA	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
10/05/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,840	CALIGIURI ET AL.	
	Examiner	Art Unit	
	ANNA PAGONAKIS	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-107* is/are pending in the application.

4a) Of the above claim(s) *43,44,48-51,53-56,61,62 and 66-107* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-42,45-47,52,57-60 and 63-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4 sheets, 12/1/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Group I, claims 39-73 as well as:

(i) absence of a taxane;

(ii) prostate cancer;

(iii) absence of an anti-cancer therapeutic co-agent.

in the reply filed on 6/2/2009 is acknowledged.

Applicant's traversal is on the grounds that all claims together in one application would not place a serious burden on the Patent Office. This is not found persuasive. Firstly, burden is not a basis for determination of Lack of Unity. With regard to Applicant's allegation that 37 C.F.R. 1.475 has been met, this is not found persuasive. As stated in the Lack of Unity mailed on 3/31/2009, a special technical feature does not exist since the compound of claim 39 is not novel, and therefore lack of unity exists. In the instant case the product linking the process claims and product claims is known to the art and as such the feature linking the groups of inventions is not special within the meaning of PCT Rule 13.2. Consequently, the methods and associated pharmaceutical compositions a priori lack unity of invention. Please note , the printed matter on a label or package insert does not lend patentable weight as a limitation of the claimed product, composition, or article of manufacture, absent a functional relationship between the label or package insert and the product, composition, or article of manufacture. See In re Haller 73 USPQ 403 (CCPA 1947), where it is held that application of printed matter to old article cannot render the article patentable.

Finally, the consideration for patentability is different in each case. Claims 39-107 are pending in the application. Claims 43-44, 48-51, 53-56, 61-62, 66-107 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter, there being no allowable generic or linking claim.

Claims 39-44, 45-47, 52, 57-62 and 63-65 are currently under examination and the subject of this Office Action.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 39-44, 45-47 and 59-60 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of a resistance or refractoriness to prostate cancer to taxane wherein the resistance or refractorness is **not mediated by tubulin or an ABC transporter** , does not reasonably provide enablement for resistance or refractoriness to prostate cancer mediated through tubulin or overexpression of an ABC transporter. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir., 1988) as to undue experimentation. The factors include:

1) the nature of the invention;
2) the breadth of the claims;
3) the predictability or unpredictability of the art;
4) the amount of direction or guidance presented;
5) the presence or absence of working examples;
6) the quantity of experimentation necessary;
7) the state of the prior art; and,
8) the relative skill of those skilled in the art.

The relevant factors are addressed below on the basis of comparison of the disclosure, the claims

and the state of the prior art in the assessment of undue experimentation.

The presently claimed invention is directed a method for treating an individual with a prostate tumor resistant or refractory to a taxane, specifically mediated through tubulin or overexpression of an ABC transporter, comprising administering the compound of claim 39. However, the instant specification as originally filed lacks adequate guidance, direction or discussion to apprise the skilled artisan how the claimed compound may be used to achieve the disclosed utilities for treatment of prostate cancer via mediation of tubulin or overexpression of an ABC transporter, with at least a reasonable expectation of successfully achieving the treatment of the same. The instant specification fails to present any evidence, either in the form of data or scientifically sound reasoning, which would provide such a reasonable expectation that the claimed compounds would have been effective for the claimed mechanistic effects.

In the instant case, Applicant has provided several examples in the specification including:

(i) efficacy of satraplatin and its metabolites is maintained in taxane-resistant tumor cells;

(ii) efficacy of satraplatin and its metabolites is maintained in camptothecin-resistant tumor cells;

(iii) efficacy of satraplatin and its metabolites is maintained in tumor cells in which resistance is mediated through ATP-binding cassette (ABC) transporters;

(iv) efficacy of satraplatin and its metabolites is maintained in cisplatin-resistant tumor cells.

Notably, however, the purported effect and/or specific interaction of the instantly claimed compounds for the mediation tubulin or overexpression of an ABC transporter of a prostate cancer is never described within the four corners of the instant specification. Though Applicant's examples in this regard are duly noted, Applicant has failed to demonstrate that the instantly claimed compounds actually functions to achieve the disclosed therapeutic use of treatment of prostate mediated through tubulin or overexpression of an ABC transporter. The specification fails to present either view a working or prophetic example(s) or a clear, scientifically sound explanation as to what, in fact, enables through

tubulin or overexpression of an ABC transporter of a prostate cancer, such that the skilled artisan would have been imbued with at least a reasonable expectation of predictability of action in using the instantly claimed compound for use in treating any one or more of the disorders disclosed as being responsive to such an effect. Absent such guidance, the experimentation required to determine if there is any activity of any of the satraplatin in prostate cancer mediation of tubulin or overexpression of an ABC transporter, and further, to determine, without needing to resort to random speculation, what therapeutic amounts would be available to even start testing for a therapeutic effect, would clearly be undue. Further, it is noted that, while the lack of a working embodiment cannot be the *sole* factor in determining enablement, the absence of substantial evidence commensurate in scope with the breadth of the presently claimed subject matter, in light of the unpredictable nature of the chemical and pharmaceutical arts and the limited direction that Applicant has presented, provides additional weight to the present conclusion of insufficient enablement in consideration of the *Wands* factors as a whole.

In the absence of such discussion or evidence, it is clear that the instant specification fails to support the enablement of treatment of prostate cancer mediation of tubulin or overexpression of an ABC transporter, such that the skilled artisan would have reasonably expected that the instantly claimed compound, effective in this manner, would have functioned to achieve the disclosed utility.

As stated in MPEP §2164.04[R-1], "Doubt may arise about enablement because information is missing about one or more essential parts or relationships between parts which one skilled in the art could not develop without undue experimentation." In the instant case, the information that is missing is a clear correlation between the claimed compound and its efficacy in treating the disclosed conditions, either through specific evidence in the form of data demonstrating such a fact or at least a sound mechanistic correlation between the claimed compound, *its ability to function in such a manner* and the amenability of the claimed disease state to treatment using an agent capable of functioning in this manner. Though one of skill in the art might very well known how to treat a patient with the claimed compound once a

diagnosis had been made of the claimed disorder (e.g., prostate cancer, etc.), it remains that the instant specification conspicuously fails to provide any guidance or direction in support of the *reasonable expectation of success* in actually effecting the mediation through tubulin or overexpression of an ABC transporter using the instantly claimed compound in the absence of any evidence supporting the allegation that the claimed compound is, in fact, effective to achieve such a therapeutic objective, either by reduction to practice or at least by elucidating the mechanism by which the claimed compound works and correlating such activity to therapeutic improvement of the disclosed disorders or diseases. In the absence of this information, the specification fails to provide adequate guidance and/or direction to one of skill in the art at the time of the invention that would have enabled such a person to practice the instantly claimed invention without having to resort to undue experimentation to determine how, in fact, one would achieve the instantly disclosed therapeutic objective(s).

The basis for the present rejection is not simply that experimentation would be required, since it is clear from the state of the prior art and Applicant's disclosure and remarks that experimentation in this particular art is not at all uncommon, but that the experimentation required in order to practice the full scope of the invention would be *undue*. Please reference *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976), which states, "The test of enablement is not whether any experimentation is necessary, but whether, *if experimentation is necessary, it is undue*." (emphasis added) Accordingly, in the absence of any adequate disclosure, direction or guidance as to how one would go about using the instantly claimed compound with a reasonable expectation of successfully treating prostate cancer mediated through tubulin, multidrug resistance or overexpression of an ABC transporter, it remains that the pharmaceutical, chemical and medical arts are notoriously complex such that methods of use would have been sufficiently unpredictable to warrant the need for undue experimentation to actually practice the full scope of the invention as instantly claimed.

In view of the discussion of each of the preceding seven factors, the level of skill in the art is high

and is at least that of a medical doctor or scientist with several years of experience in the art.

As the cited art and discussion of the above factors establish, practicing the claimed method in the manner disclosed by Applicant would not imbue the skilled artisan with a reasonable expectation or ability to make and use the full scope of the invention as instantly claimed, given the disclosure and supporting examples provided in the present specification and the state of the art at the time of the invention. In order to actually achieve the claimed invention, it is clear from the discussion above that the skilled artisan could not rely upon Applicant's disclosure as required by 35 U.S.C. 112, first paragraph, and would have no alternative recourse but the impermissible burden of undue experimentation in order to practice the full scope of the embodiments presently claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 39-44, 45-47, 52, 57-62 and 63-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jia (U.S. 6,759,397) and Bednarski (Current Opinion Oncol., Endocr. Metab. Invest Drugs, 1999) in view of Rowsinky et al. (New England Journal of Medicine, 1995) and Masferrer (U.S. 2004/0072889).

Jia et al. teaches that cisplatin and Rh2 is administered to non-Pgp containing multidrug resistant prostate cancer and are synergistic. Jia et al. also teach the administration of cisplatin and Rh2 to multidrug non PgP resistatn mesothelioma cells is synergistic (column 7, example 3).

Jia et al. is silent on the administration of JM216 to paclitaxel resistant cells.

Bednarski et al. teaches that JM216, the elected compound, is in phase III clinical trails investigating its potential for treating prostate cancer (page 1, column 1). The specification states that alternative names for the instantly claimed compound of claim 1 include JM216 and satraplatin (see page 10 of specification).

Bednarski et al. is silent on the administration to a patient population that is taxane resistant or refractory.

Rowinsky et al. teaches that paclitaxel is a well known taxane (column 1, page 1004).

Masferrer teaches that cisplatin and satraplatin are both platin antineoplastic agents (paragraph [1108]).

It would have been obvious to administer to multidrug resistant prostate cancer patients the combination of cisplatin /Rh2 and JM216 because Jia et al. teach that cisplatin/Rh2 is synergistic in non Pgp multiple drug resistant cells and JM216 has potential for the treatment of prostate cancer. Further, one skilled in the art would have been motivated to substitute the functionally equivalent satraplatin for cisplatin since each is a related platin compound.

Conclusion

No claim is found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNA PAGONAKIS whose telephone number is (571)270-3505. The examiner can normally be reached on Monday thru Thursday, 9am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AP

/Patricia A. Duffy/
Primary Examiner, Art Unit 1645